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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,025	03/31/2004	James Rasmussen	GC22.4-CON2	4968

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EXAMINER	
SULLIVAN, DANIEL M	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/814,025	RASMUSSEN ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *48-72* is/are pending in the application.

4a) Of the above claim(s) *48-59 and 67-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *60-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This is the First Office Action on the Merits of the application filed 31 March 2004 as a continuation of application 09/995,337 filed 27 November 2001, which is a continuation of application 08/442,603 filed 17 May 1995, which is a continuation of application 08/015,735, which is a continuation of application 07/748,283 filed 21 August 1991, which is a divisional of application 07/445,507 filed 22 December 1989, which is a continuation-in-part of application 07/289,589 filed 23 December 1988. The preliminary amendments filed 31 March 2004, 3 June 2004, 4 August 2004, and 1 June 2005 have been entered. Claims 1-47 were originally filed. Claims 2-47 were canceled in the 31 March Paper. Claim 1 was canceled and claims 48-72 were added in the 3 June Paper. Claim 60 was amended in the 1 June Paper. Claims 48-72 are presently pending.

Election/Restrictions

Applicant's election with traverse of Group II (claims 60-66) in the interview summarized in the 23 June 2005 Paper and the species wherein the inhibitor is deoxy-mannojirimycin in the paper filed on 1 June 2005 is acknowledged.

Applicant traverses the restriction of Groups I and II, directed to a process of making and product made, on the grounds that the composition of Group II could not be produced by a different method because the claims of Group II recite that the product is produced by the method recited in Group I.

This is not found persuasive because it is well established in patent law that a product claimed as a product-by-process of making reads on the product made by any means. *In re*

Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) states: "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Thus, the product of Group II is not, in fact, limited to being produced by the process of Group I. Instead, it encompasses any product that might be made by that process regardless of the process actually used to produce the product.

Applicant traverses the restriction of Groups II and III, directed to a product and process of using, on the grounds that the product claims recite that the glucocerebrosidase is "useful for the treatment of a human patient having Gaucher's disease". This argument is not persuasive because a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). Thus, the claimed products read on any glucocerebrosidase having the disclosed properties of the claimed product regardless of whether the glucocerebrosidase is disclosed as used in a therapeutic method. Therefore, absent evidence to the contrary, a glucocerebrosidase disclosed as useful as a standard in an assay would read on the claims.

Finally, Applicant traverses the restriction of Groups I and III on the grounds that the claims of Group I recite that the glucocerebrosidase produced thereby is useful for the treatment

of a human patient having Gaucher's disease as recited in the claims of Group III. However, as stated in the restriction requirement (page 4) each method is limited to comprising elements to which the other method is not limited and because each method encompasses subject matter not encompassed by the other method, a determination that any one method is patentable over the art does not adequately support patentability of the other method. Therefore, patentability of each method must be determined separately.

With regard to the species election, Applicant states that the Examiner has presented no evidence to support the assertion that the inhibitors of carbohydrate processing would produce glucocerebrosidase enzymes having distinct structural and functional properties and contends that the inhibitors of the claims will produce glucocerebrosidases with improved binding to mannose receptors.

First, with regard to evidence, the attached product inserts describing 1-deoxymannojirimycin, deoxy-nojirimycin, swainsonine and castanospermine indicate that each inhibitor acts to inhibit distinct cellular enzymes, which, absent evidence to the contrary, would clearly result in glucocerebrosidase enzymes having distinct glycosylation patterns. If it is Applicant's position that the species are not patentably distinct, Applicant is again invited to submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case.

The requirement is still deemed proper and is therefore made FINAL.

Claims 48-59 and 67-72 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and claims 63-66 are withdrawn from further

consideration as being drawn to nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the 1 June Paper.

Claims 60-62 are presently under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 60-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

The claims are directed to a composition comprising a glucocerebrosidase wherein the glucocerebrosidase is produced by a process wherein cells expressing a glucocerebrosidase are

treated with an inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$ to smaller species.

The specification teaches that the glucocerebrosidase of the claims encompasses all enzymes having an enzyme activity which causes hydrolysis of a glucocerebroside (page 6, lines 31-33). Thus, the claims encompass any enzyme having glucocerebrosidase activity regardless of the structure thereof. Furthermore, the specification teaches that the claimed glucocerebrosidase can be the product of a glucocerebrosidase produce by introducing a GCR-encoding DNA into cell and treating the cell with any inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$ to smaller species. Thus, the claims encompass a highly divergent genus encompassing any polypeptide capable of hydrolyzing a glucocerebroside isolated from any mammalian cell wherein conversion of $Glc_3Man_9GlcNac_2$ to smaller species has been inhibited.

The Guidelines for Written Description state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (Federal Register, Vol. 66, No. 4, Column 3, page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" (MPEP §2163(3)(a)(ii)).

The teachings in the specification with regard to a glucocerebrosidase produced by the method recited in the claims are prophetic. The working Examples describe expression of a glucocerebrosidase in insect and Chinese hamster ovary (CHO) cells and the carbohydrate structure of the resultant glucocerebrosidase from SF9 cells (see especially the discussion beginning on page 23). Although, in the first full paragraph on page 2, the application cites two papers as disclosing the sequence of a gene encoding a human GCR, the structural characteristics defining the broad genus of any enzyme having an activity which causes hydrolysis of a glucocerebroside were not conventional in the art and are not disclosed in the instant application. In fact, the only disclosure of an enzyme having the activity of a glucocerebrosidase is in the form of expression constructs that comprise an enzyme having glucocerebrosidase activity (*i.e.*, pGB20, described in Figure 7, pGB37, described in Figure 9-2, and pGB42, described in Figure 9.2).

The specification teaches, prophetically, that rGCR having an appropriate carbohydrate structure can be produced by introducing GCR-encoding DNA into any vertebrate or invertebrate cell and treating the cell with inhibitors of carbohydrate processing (bridging pages 27-28). However, the specification also teaches that, to be therapeutically useful as recited in the claims, the glucocerebrosidase must be post-translationally modified to provide a carbohydrate structure which will target to human mannose receptors (see especially the paragraph bridging page 26-27). The specification further teaches that such a glucocerebrosidase has at least two carbohydrate moieties each having a Man_3-Man_9 structure and such rGCR represents at least 50% of the rGCR provided in the therapeutic composition (page 27, lines 1-4). However, the specification provides no specific disclosure of which combination within the broad scope of a

glucocerebrosidase produced by any mammalian cell exposed to any inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$ to smaller species will comprise the requisite carbohydrate structure. The art recognizes that the factors determining the glycosylation pattern of a polypeptide in any given mammalian cell are complex and unpredictable, particularly when the polypeptides are produced in the amounts sufficient for pharmaceutical use. For example, Houdebine *et al.* (2000) *Transgen. Res.* 9:305-320 (made of record in the IDS filed 31 March 2004) teaches proper posttranslational processing of proteins expressed at pharmaceutically relevant levels is often unpredictable because the mechanisms are dependent on cellular enzymes that are present at variable concentrations in different cell types (paragraph bridging the left and right columns on page 313). Houdebine further teaches that mammary cells do not always glycosylate recombinant proteins in an appropriate manner even when the protein is secreted in milk in a glycosylated form (see the example of bile salt-stimulated lipase presented in the second full paragraph in the right column on page 313). Houdebine teaches that the reasons why some proteins are not correctly glycosylated are particularly complex and might be related to the superphysiological production of the recombinant proteins.

Beyond the scope of a CHO cell comprising an enzymatically active human glucocerebrosidase, said cell being transformed with a plasmid selected from the group consisting of PGB20, PGB37 and PGB42, the application fails to disclose the properties of any enzyme produced by the method recited in the claims such that the skilled artisan would recognize that applicant was in possession of any glucocerebrosidase enzyme produced by any cell from any of the more than 5,000 species of mammal, wherein the cell is exposed to any

inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$ and wherein the glucocerebrosidase has the properties identified as critical to use in the treatment of Gaucher's disease in a human patient.

Although the application discloses a method by which the desired activity might be identified, an adequate written description of a molecule requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the glucocerebrosidase itself. It is not sufficient to define an enzyme solely by its principal biological property (*i.e.* it has an enzyme activity which causes hydrolysis of a glucocerebroside and is useful in the treatment of Gaucher's disease in humans) because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any glucocerebrosidase with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all glucocerebrosidases that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

In view of the tremendous scope of the claims, the unpredictable nature of glycosylation in mammalian cells and the failure of the specification to provide a detailed description of the claimed invention beyond the scope of a CHO cell transformed with a plasmid selected from the group consisting of PGB20, PGB37 and PGB42, the skilled artisan would conclude that Applicant was not in possession of the full scope of the claimed invention at the time the application was filed.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 60-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: As described above, the claims are directed to a composition comprising a glucocerebrosidase wherein the glucocerebrosidase is produced by a process wherein cells expressing a glucocerebrosidase are treated with an inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$ to smaller species. Viewed in light of the disclosure, the claims encompass any polypeptide capable of hydrolyzing a glucocerebroside isolated from any mammalian cell wherein conversion of $Glc_3Man_9GlcNac_2$ to smaller species has been inhibited. Further, the claims recite either that the

glucocerebrosidase is useful for the treatment of Gaucher's disease or is a component of a pharmaceutical composition. Thus, the enabling disclosure must teach the skilled artisan how to make the claimed invention such that it can be used as a pharmaceutical.

Amount of direction provided by the inventor and existence of working examples: As discussed above, the teachings in the specification with regard to a glucocerebrosidase produced by the method recited in the claims are prophetic. The working Examples describe expression of a glucocerebrosidase in insect and Chinese hamster ovary (CHO) cells and the carbohydrate structure of the resultant glucocerebrosidase from SF9 cells (see especially the discussion beginning on page 23). Although, in the first full paragraph on page 2, the application cites two papers as disclosing the sequence of a gene encoding a human GCR, the structural characteristics defining the broad genus of any enzyme having an activity which causes hydrolysis of a glucocerebroside were not conventional in the art and are not disclosed in the instant application. In fact, the only disclosure of an enzyme having the activity of a glucocerebrosidase is in the form of expression constructs that comprise an enzyme having glucocerebrosidase activity (*i.e.*, pGB20, described in Figure 7, pGB37, described in Figure 9-2, and pGB42, described in Figure 9.2).

The specification teaches, prophetically, that rGCR having an appropriate carbohydrate structure can be produced by introducing GCR-encoding DNA into any vertebrate or invertebrate cell and treating the cell with inhibitors of carbohydrate processing (bridging pages 27-28). However, the specification also teaches that, to be therapeutically useful as recited in the claims, the glucocerebrosidase must be post-translationally modified to provide a carbohydrate structure which will target to human mannose receptors (see especially the paragraph bridging page 26-

27). The specification further teaches that such a glucocerebrosidase has at least two carbohydrate moieties each having a Man_3-Man_9 structure and such rGCR represents at least 50% of the rGCR provided in the therapeutic composition (page 27, lines 1-4). However, the specification provides no specific disclosure of which combination within the broad scope of a glucocerebrosidase produced by any mammalian cell exposed to any inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$ to smaller species will comprise the requisite carbohydrate structure.

With regard to therapeutic application of the claimed invention, the specification merely teaches, "[t]he rGCR of the invention is suitable for administration to a human suffering from Gaucher's disease using a standard enzyme replacement protocol" (third full paragraph on page 5).

State of the prior art and level of predictability in the art: With regard to making the full scope of what is presently claimed, the art does not disclose the structural features of glucocerebrosidase enzymes as claimed such that the skilled artisan would know how to make any protein having an enzyme activity which causes hydrolysis of a glucocerebroside. Furthermore, as discussed above, the art recognizes that the factors determining the glycosylation pattern of a polypeptide in any given mammalian cell are complex and unpredictable, particularly when the polypeptides are produced in the amounts sufficient for pharmaceutical use. For example, Houdebine *et al.* (2000) *Transgen. Res.* 9:305-320 (made of record in the IDS filed 31 March 2004) teaches proper posttranslational processing of proteins expressed at pharmaceutically relevant levels is often unpredictable because the mechanisms are dependent on cellular enzymes that are present at variable concentrations in different cell types (paragraph

bridging the left and right columns on page 313). Houdebine further teaches that mammary cells do not always glycosylate recombinant proteins in an appropriate manner even when the protein is secreted in milk in a glycosylated form (see the example of bile salt-stimulated lipase presented in the second full paragraph in the right column on page 313). Houdebine teaches that the reasons why some proteins are not correctly glycosylated are particularly complex and might be related to the superphysiological production of the recombinant proteins

With regard to pharmaceutical application, the art teaches that, as of the effective filing date of the instant application (*i.e.,* 23 December 1988) there was no standard enzyme replacement protocol for Gaucher's disease. For example, Beutler *et al.* (1991) *Blood* 78:1183-1189 teaches, "[a]lthough a number of attempts to treat Gaucher disease by enzyme replacement were made in the 1970s, these were unsuccessful" (second paragraph on page 1183). Although Beutler *et al.* discloses an enabled enzyme replacement method, the disclosure of Beutler *et al.*, including an effective dosage and route of administration, was not available to the skilled artisan at the time the instant application was filed.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to make and use the claimed invention based on the instant disclosure and the teachings available in the art. The claims are tremendously broad, encompassing any polypeptide capable of hydrolyzing a glucocerebroside isolated from any mammalian cell wherein conversion of $Glc_3Man_9GlcNac_2$ to smaller species has been inhibited. However, given the absence of an adequate disclosure of the features that define a genus of any polypeptide capable of hydrolyzing a glucocerebroside and the unpredictability of glycosylation in mammalian cells, the skilled

artisan would have to make and test each species within an essentially unlimited genus of polypeptides for the function recited in the claims. Furthermore, with regard to therapeutic application, given that there was no established enzyme replacement therapy for Gaucher's disease at the time the application was filed and the absence of any specific teachings with regard to effective enzyme replacement therapy, the skilled artisan would have to develop an effective therapy experimentally. Given the high degree of unpredictability that is a general feature of developing any effective therapy, the amount of experimentation required to develop the invention such that it could be made and used as recited in the claims would be undue.

For these reasons, the skilled artisan would not be able to make and use the claimed invention without undue experimentation. Therefore, the claims are properly rejected under 35 USC §112, first paragraph.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 60-62 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,451,600. Although the conflicting claims are not identical, they are not patentably distinct from each other. The instant claims are directed to compositions comprising a glucocerebrosidase produced by a method comprising providing a culture of mammalian cells capable of expressing a glucocerebrosidase and treating cells with an inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$. The claimed composition is generic to all that is claimed in claim 1 of the '600 patent, which is directed to a CHO cell comprising nucleic acids encoding an enzymatically active human glucocerebrosidase, except that the claim does not require that the glucocerebrosidase is the product of a cell exposed to an inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$. However, this limitation would have been obvious to one of ordinary skill in the art based on the disclosure of the '600 patent, which teaches that rGCR having an appropriate carbohydrate structure can be produced by introducing GCR-encoding DNA into a vertebrate cell and treating the cell with inhibitors of carbohydrate processing such as deoxy-mannojirimycin (column 14, lines 24-35). In view of this teaching, the skilled artisan would be motivated to treat the cell of claim 1 with an inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$ to produce a glucocerebrosidase having an appropriate structure.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 60-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Aerts *et al.* (1986) *Biochem. Biophys. Res. Commun.* 141:452-458.

The claims are directed to a glucocerebrosidase produced by a method comprising providing a culture of mammalian cells capable of expressing a glucocerebrosidase, treating said cells with an inhibitor of carbohydrate processing that acts to inhibit conversion of $Glc_3Man_9GlcNac_2$ and recovering the glucocerebrosidase from said culture, wherein said recovered glucocerebrosidase contains a higher number of exposed mannose residues than does human placental glucocerebrosidase.

Aerts *et al.* teaches culturing U937 cells (a human monocyte cell line) in the presence of deoxy-mannojirimycin and recovering a glucocerebrosidase from the cultured cells (see especially the paragraph bridging pages 453-454, the first full paragraph on page 455, the paragraph bridging pages 455-456 and Figure 2 and the caption thereto). As the process of making the glucocerebrosidase of Aerts *et al.* is the same as the process recited in the instant claims, the skilled artisan would recognize that the product made thereby is the same as the product presently claimed. The Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re*

Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989).

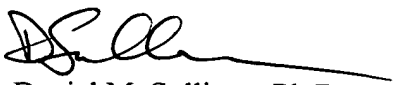
For these reasons, the claims are anticipated by Aerts *et al.*

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Daniel M. Sullivan, Ph.D.
Examiner
Art Unit 1636